SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Furosemide Tablets 40mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 40 mg of Furosemide.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, flat bevelled edge tablets engraved with company logo on one side and a breakline and A270 on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Furosemide is a diuretic recommended for use in all indications where a prompt and effective diuresis is required.

1) The treatment of oedema associated with congestive heart failure, cirrhosis of the liver, renal disease including nephrotic syndrome and pulmonary oedema.

2) The treatment of peripheral oedema due to mechanical obstruction, venous insufficiency, mild to moderate hypertension.

4.2 Posology and method of administration

Route of administration: Oral

Furosemide has a very wide therapeutic range, the effect being proportional to dosage.
Furosemide is best given as a single dose either daily or on alternate days.

Adults and children over 12 years:
Oedema: Initially 40mg daily in the morning; ordinarily a prompt diuresis ensues and the starting dose can then be maintained or even reduced. Diuresis lasts for approximately four hours following administration and hence the time of administration can be adjusted to suit the patient's requirements. Maintenance dose is 20mg daily or 40mg on alternate days, increased in resistant oedema to 80mg daily.
Hypertension: 20-40mg twice daily; if 40mg twice daily does not lead to a clinically satisfactory response, the addition of other antihypertensive agents, rather than an increase in the dose of furosemide should be considered.

Children under 12 years:
1-3 mg/kg body weight daily. A more suitable dosage form should be used in this age group.

Elderly:
In the elderly, furosemide is generally eliminated more slowly. Dosage should be titrated until the required response is achieved.

4.3 Contraindications

Known hypersensitivity to furosemide, amiloride or any of the excipients of the product.
Known hypersensitivity to sulphonamides and sulphonamide derivatives.
Anuria or renal failure with anuria not responding to furosemide.
Electrolyte deficiency.
Comatose or pre-comatose states associated with liver cirrhosis (see section 4.4);
Digitalis intoxication (see section 4.5).
Renal failure resulting from nephrotoxic and hepatotoxic agents.
Renal failure associated with hepatic coma.
Hypovolaemia and dehydration (with or without accompanying hypotension) (see section 4.4)
Severe hypokalaemia: severe hyponatraemia (see section 4.4).
Impaired renal function with a creatinine clearance below 30ml/min per 1.73 m² body surface area (see section 4.4).
Addison's disease (see section 4.4).

Children and adolescents under 18 years of age (safety in this age group has not yet been established).

Porphyria

Concomitant potassium supplements or potassium sparing diuretics (see section 4.5).

Breast-feeding women (see section 4.6).

4.4 Special warnings and precautions for use

Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

Conditions requiring correction before furosemide is started (see also section 4.3):

- Hypotension and hypovolaemia
- Severe electrolyte disturbances - particularly hypokalaemia, hyponatraemia and acid-base disturbances.

Furosemide is not recommended:

- In patients at high risk for radiocontrast nephropathy - it should not be used for diuresis as part of the preventative measures against radiocontrast-induced nephropathy.

Particular caution and/or dose reduction required:

- elderly patients (lower initial dose as particularly susceptible to side-effects - see section 4.2).
- patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute retention: consider lower dose.
- closely monitor patients with partial occlusion of the urinary tract.
- diabetes mellitus (latent diabetes may become overt: insulin requirements in established diabetes may increase: stop furosemide before a glucose tolerance test).
- pregnancy (see section 4.6).
- serum creatinine and uric acid/urea levels tend to rise during treatment with furosemide and an acute attack of gout may occasionally be precipitated.
- patients with hepatorenal syndrome
- impaired hepatic function (see section 4.3 and below - monitoring required).
- impaired renal function (see section 4.3 and below - monitoring required).
• adrenal disease (see section 4.3 - contraindication in Addison's disease).
• hypoproteinaemia e.g. nephrotic syndrome (effect of furosemide may be impaired and its ototoxicity potentiated - cautious dose titration required).
• acute hypercalcaemia (dehydration results from vomiting and diuresis - correct before giving furosemide). Treatment of hypercalcaemia with a high dose of furosemide results in fluid and electrolyte depletion - meticulous fluid replacement and correction of electrolyte required.
• the dosage of concurrently administered cardiac glycosides or antihypertensive agents may require adjustment.
• patients who are at risk from a pronounced fall in blood pressure
• premature infants (possible development nephrocalcinosis/nephrolithiasis; renal function must be monitored and renal ultrasonography performed)
• Symptomatic hypotension leading to dizziness, fainting or loss of consciousness can occur in patients treated with furosemide, particularly in the elderly, patients on other medications which can cause hypotension and patients with other medical conditions that are risks for hypotension..

Avoidance with other medicines (see also section 4.5 for other interactions):
• concurrent NSAIDs should be avoided - if not possible diuretic effect of furosemide may be attenuated.
• ACE-inhibitors & Angiotensin II receptor antagonists - severe hypotension may occur - dose of furosemide should be reduced/stopped (3 days) before starting or increasing the dose of these.

Laboratory monitoring requirements:
• Serum sodium
Particularly in the elderly or in patients liable to electrolyte deficiency.

• Serum potassium
The possibility of hypokalaemia should be taken into account, in particular in patients with cirrhosis of the liver, those receiving concomitant treatment with corticosteroids, those with an unbalanced diet and those who abuse laxatives. Regular monitoring of plasma electrolytes, particularly sodium and potassium should be carried out and electrolyte replacement therapy instituted accordingly, and if necessary treatment with a potassium supplement, is recommended in all cases, but is essential at higher doses and in patients with impaired renal function. It is especially important in the event of concomitant treatment with digoxin, as potassium deficiency can trigger or exacerbate the symptoms of digitalis intoxication (see section 4.5). Caution should be observed in patients liable to electrolyte deficiency. During long-term or high dose therapy potassium supplements are recommended.

Frequent checks of the serum potassium are necessary in patients with impaired renal function and creatinine clearance below 60ml/min per 1.73m² body surface area as well as in cases where furosemide is taken in combination with certain other drugs which may lead to an increase in potassium levels (see section 4.5 & refer to section 4.8 for details of electrolyte and metabolic abnormalities).
• Renal function
Marked diuresis can cause reversible impairment of kidney function in patients with renal dysfunction. Frequent BUN determinations during the first few months of therapy and periodically thereafter should be conducted. Long-term/high-dose BUN should regularly be measured. Adequate fluid intake is necessary in such patients. Serum creatinine and urea levels tend to rise during treatment.

• Glucose
Adverse effect on carbohydrate metabolism - exacerbation of existing carbohydrate intolerance or diabetes mellitus. Regular monitoring of blood glucose levels is desirable.

• Other electrolytes
Patients with hepatic failure/alcoholic cirrhosis are particularly at risk of hypomagnesia (as well as hypokalaemia). During long-term therapy (especially at high doses) magnesium, calcium, chloride, bicarbonate and uric acid should be regularly measured.

Clinical monitoring requirements:

Regular observations for possible occurrence of blood dyscrasias (If these occur, stop Furosemide immediately), liver damage or idiosyncratic reactions are advisable.

Other alterations in lab values:

Serum cholesterol and triglyceride levels may rise during furosemide treatment but will usually return to normal within six months of starting furosemide.

Care needs to be taken when prescribing to patients with porphyria as furosemide may induce acute porphyric crisis.

Concomitant use with risperidone
In risperidone placebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone (7.3%; mean age 89 years, range 75-97 years) when compared to patients treated with risperidone alone (3.1%; mean age 84 years, range 70-96 years) or furosemide alone (4.1%; mean age 80 years, range 67-90 years). Concomitant use of risperidone with other diuretics (mainly thiazide diuretics used in low dose) was not associated with similar findings.

No pathophysiological mechanism has been identified to explain this finding, and no consistent pattern for cause of death observed. Nevertheless, caution should be exercised and the risks and benefits of this combination or co-treatment with other potent diuretics should be considered prior to the decision to use. There was no increased incidence of mortality among patients taking other diuretics as concomitant treatment with risperidone. Irrespective of treatment, dehydration was an overall risk factor for mortality and should therefore be avoided in elderly patients with dementia (see section 4.3 Contraindications).

4.5 Interaction with other medicinal products and other forms of interaction
General- The dosage of concurrently administered cardiac glycosides, diuretics, anti-hypertensive agents, or other drug with blood-pressure-lowering potential may require adjustment as a more pronounced fall in blood pressure must be anticipated if given concomitantly with furosemide.

The toxic effects of nephrotoxic drugs may be increased by concomitant administration of potent diuretics such as furosemide.

Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).

Antihypertensives (ACE Inhibitors and Angiotensin-II Antagonists): concomitant administration with furosemide can result in marked falls in blood pressure. This enhancement may be extreme. The dose of furosemide should be reduced or the drug stopped before initiating the ACE inhibitor or Angiotensin II receptor antagonists (see section 4.4).

Antihypertensives: enhanced hypotensive effect; increased risk of first-dose hypotensive effect of post synaptic alpha-blockers such as prazosin.

Alcohol: enhanced hypotensive effect when diuretics are given with alcohol.

Aminoglutethimide: increased risk of hyponatraemia with aminoglutethimide.

Antifungals/Amphotericin: there is an increased risk of hypokalaemia and nephrotoxicity.

NSAIDs/Analgesics: there is an increased risk of nephrotoxicity of NSAIDs. Some NSAIDs (Indometacin and ketorolac) and salicylates antagonise the diuretic effect (avoid if possible; see section 4.4), and the effects of salicylates may be potentiated by furosemide. Salicylic toxicity may be increased.

Anti-arrhythmics: the risk of cardiac toxicity of amiodarone, disopyramide, flecainide, sotalol and quinidine may increase if furosemide induced hypokalaemia occurs. The effects of lidocaine, tocainide or mexiletine may be antagonised by furosemide.

Antibacterials: concomitant administration of loop diuretics may increase ototoxicity of aminoglycosides, colistin, polymixins or vancomycin - only use concurrently if compelling reasons. Loop diuretics may increase nephrotoxicity of cephalosporins (including cefaloridine) or aminoglycosides. Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins. Furosemide can decrease vancomycin serum levels after cardiac surgery. Increased risk of hyponatraemia with trimethoprim.

Antidepressants: there is an increased risk of postural hypotension with concomitant administration of furosemide and tricyclic antidepressants. Concomitant administration of loop diuretics with reboxetine may increase the risk of hypokalaemia; there is an enhanced
hypotensive effect with concomitant administration with MAOIs.

Antidiabetics: the hypoglycaemic effect of antidiabetics is antagonised by loop diuretics. (see section 4.4).

Anaesthetics, General: enhanced hypotensive effect when diuretics are given with general anaesthetics. The effects of curare may be enhanced by furosemide.

Antiepileptics: effects of furosemide antagonised by phenytoin.
Carbamazepine: there is an increased risk of hyponatraemia.

Antihistamines - hypokalaemia with increased risk of cardiac toxicity.
Terfenidine: hypokalaemia or other electrolyte imbalance increases the risk of ventricular arrhythmias

Anxiolytics and hypnotics- enhanced hypotensive effect. Choral or triclofos may displace thyroid hormone from binding site.
CNS stimulants (drugs used for ADHD) - hypokalaemia increases the risk of ventricular arrhythmias.

Antipsychotics: Furosemide induced hypokalaemia increases the risk of cardiac toxicity. Avoid concurrent use with pimozide or thioridazine. Increased risk of ventricular arrhythmias with amisulpride or sertindole. Enhanced hypotensive effect with phenothiazines.

When administering risperidone, caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use. See section 4.4 Special warnings and precautions for use regarding increased mortality in elderly patients with dementia concomitantly receiving risperidone.

Beta-blockers: enhanced hypotensive effect.

Calcium-channel blockers: enhance hypotensive effect.

Cardiac glycosides: there is increased risk of cardiac toxicity if hypokalaemia and electrolyte disturbances (including hypomagnesia) occurs with furosemide.
Drugs that prolong Q-T interval - increased risk of toxicity with furosemide-induced electrolyte disturbances.

Renin inhibitors - aliskiren reduces plasma concentrations of furosemide.

Nitrates - enhanced hypotensive effect.
Corticosteroids e.g. glucocorticoids: increased risk of hypokalaemia with loop diuretics. Antagonism of diuretic effect (sodium retention).

Glycyrrhizin (contained in liquorice) - may increase the risk of developing hypokalaemia.

Cytotoxics: increased risk of nephrotoxicity and ototoxicity with platinum compound/cisplatin. Nephrotoxicity of cisplatin may be enhanced if furosemide is not given in low doses (e.g. 40 mg in patients with normal renal function) and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.

Anti-metabolites - effects of furosemide may be reduced by methotrexate and furosemide may reduce renal clearance of methotrexate.

Potassium salts - contraindicated - increased risk of hyperkalaemia (see section 4.3)

Dopaminergics - enhanced hypotensive effect with levodopa.

Immunomodulators - enhanced hypotensive effect with aldesleukin. Increased risk of hyperkalaemia with ciclosporin and tacrolimus. Increased risk of gouty arthritis with ciclosporin.

Diuretics: increased risk of hypokalaemia if acetazolamide, loop diuretics or thiazides given together; profound diuresis possible if metolazone given with furosemide. Contraindicated with potassium-sparing diuretics (e.g. amiloride, spironolactone) - increased risk of hyperkalaemia (see section 4.3).

Lithium: In common with other diuretics, serum lithium levels may be increased when lithium is administered concomitantly with furosemide, resulting in increased lithium toxicity, including increased risk of cardiotoxic and neurotoxic effects of lithium. Therefore, it is recommended that lithium levels are carefully monitored and where necessary the lithium dosage is adjusted in patients receiving this combination.

Chelating agents - sucralfate may decrease the gastrointestinal absorption of furosemide - the 2 drugs should be taken at least 2 hours apart.

Vasodilators- Moxisylyte (Thymoxamine) or hydralazine: enhance hypotensive effect.

Muscle Relaxants: enhanced hypotensive effect with baclofen and tizanidine. Increased effect of curare like muscle relaxants.

Oestrogens and Progestogens: oestrogens and combined oral contraceptives antagonise diuretic effect, Progestogens (drospirenone) increased risk of hyperkalaemia.

Prostaglandins - enhanced hypotensive effect with alprostadil.

Sympathomimetics: increased risk of hypokalaemia if loop diuretics given with high doses.
of beta₂ sympathomimetics (bambuterol, fenoterol, formoterol, ritodrine, salbutamol, salmeterol and terbutaline).

Probenecid - effects of furosemide may be reduced by probenecid and furosemide may reduce renal clearance of probenecid.

Theophylline: increased risk of hypokalaemia with loop diuretics. Enhanced hypotensive effect.

Ulcer-healing drugs: increased risk of hypokalaemia if loop diuretics are given with carbenoxolone. Carbenoxolone antagonises diuretic effect.

In cases of concomitant laxative abuse, the risk of an increased potassium loss should be borne in mind.

4.6 Pregnancy and lactation

**Pregnancy**

Experimental work carried out on animals generally shows that furosemide has no hazardous effects in pregnancy. There is no evidence of the safety of high doses of furosemide in human pregnancy. However, there is clinical evidence of safety of the drug in the third trimester of human pregnancy & furosemide has been given after the first trimester of pregnancy for oedema, hypertension and toxaemia of pregnancy without causing fetal or newborn adverse effects. Furosemide should be used in pregnancy only if strictly indicated and for short term treatment.

Furosemide crosses the placental barrier and should not be given during pregnancy unless there are compelling medical reasons. It should only be used for the pathological causes of oedema which are not directly or indirectly linked to the pregnancy. The treatment with diuretics of oedema and hypertension caused by pregnancy is undesirable because placental perfusion can be reduced, so, if used, monitoring of fetal growth is required.

**Lactation (see section 4.3)**

Furosemide is contraindicated as furosemide has an inhibiting effect on lactation and may pass into the breast milk.

4.7 Effects on ability to drive and use machines

Reduced mental alertness, dizziness and blurred vision have been reported, particularly at the start of treatment, with dose changes and in combination with alcohol. Patients should be advised that if affected, they should not drive, operate machinery or take part in activities where these effects could put themselves or others at risk.

4.8 Undesirable effects
Undesirable effects can occur with the following frequencies: very common (> 1/10), common (> 1/100, < 1/10), uncommon (> 1/1,000, < 1/100), rare (> 1/10,000, < 1/1,000) and very rare (< 1/10,000, including isolated reports).

**Blood and lymphatic system disorders:**
Uncommon: Thrombocytopenia

Rare:
- eosinophilia
- leukopenia
- bone marrow depression (necessitates withdrawal of treatment). The haemopoietic status should therefore be regularly monitored.

Very Rare:
- aplastic anaemia or haemolytic anaemia
- agranulocytosis

**Nervous system disorders**
Rare:
- paraesthesia
- hyperosmolar coma

Not known: dizziness, fainting or loss of consciousness caused by symptomatic hypotension

**Endocrine disorder**
Glucose tolerance may decrease with furosemide. In patients with diabetes mellitus this may lead to a deterioration of metabolic control; latent diabetes mellitus may become manifest. Insulin requirements of diabetic patients may increase.

**Eye disorders**
Uncommon: visual disturbance

**Ear and labyrinth disorders**
Uncommon: deafness (sometimes irreversible)

Hearing disorders, tinnitus, although usually transitory, may occur in rare cases, particularly in patients with renal failure, hypoproteinaemia (e.g. in nephritic syndrome) and/or when intravenous furosemide has been given too rapidly.

**Cardiac disorders**
Uncommon: cardiac arrhythmias

Furosemide may cause a reduction in blood pressure which, if pronounced may cause signs and symptoms such as impairment of concentration and reactions, light headedness, sensations of pressure in the head, headache, dizziness, drowsiness, weakness, disorders
of vision, dry mouth, orthostatic intolerance. The diuretic effect of furosemide can result in hypovolaemia and dehydration, especially in the elderly. There is an increased risk of thrombosis.

**Hepatobiliary disorders**
In isolated cases, intrahepatic cholestasis, an increase in liver transaminases or acute pancreatitis may develop.

Hepatic encephalopathy in patients with hepatocellular insufficiency may occur (see Section 4.3).

**Vascular Disorder:**
Rare: vasculitis

**Skin and subcutaneous tissue disorders:**
Uncommon: Photosensitivity

Rare:
Skin and mucous membrane reactions may occasionally occur, e.g. itching, urticaria, other rashes or bullous lesions, fever, hypersensitivity to light, exudative erythema multiforme (Lyell's syndrome and Stevens-Johnson syndrome), bullous exanthema, various forms of dermatitis (including exfoliative dermatitis), purpura and DRESS (Drug rash with eosinophilia and systemic symptoms).

Not known: AGEP (acute generalized exanthematous pustulosis).

When these occur, treatment with furosemide should be stopped.

**Metabolism and nutrition disorders:**
As with other diuretics, electrolytes and water balance may be disturbed as a result of diuresis after prolonged therapy. This may cause symptoms such as headache, hypotension or muscle cramps. Furosemide leads to increased excretion of sodium and chloride and consequently increased excretion of water. In addition, excretion of other electrolytes (in particular potassium, calcium and magnesium) is increased.

Metabolic acidosis can also occur. The risk of this abnormality increases at higher dosages and is influenced by the underlying disorder (e.g. cirrhosis of the liver, heart failure), concomitant medication (see section 4.5) and diet. Pre-existing metabolic alkalosis (e.g. in decompensated cirrhosis of the liver) may be aggravated by furosemide treatment.

Symptomatic electrolyte disturbances and metabolic alkalosis may develop in the form of a gradually increasing electrolyte deficit or e.g. where higher furosemide doses are administered to patients with normal renal function, acute severe electrolyte losses.

Symptoms of electrolyte imbalance depend on the type of disturbance:
Sodium deficiency can occur; this can manifest itself in the form of confusion, muscle cramps, muscle weakness, loss of appetite, dizziness, drowsiness and vomiting.

Potassium deficiency manifests itself in neuromuscular symptoms (muscular weakness, paralysis), intestinal symptoms (vomiting, constipation, meteorism), renal symptoms (polyuria) or cardiac symptoms. Severe potassium depletion can result in paralytic ileus or confusion, which can result in coma.

Magnesium and calcium deficiency result very rarely in tetany and heart rhythm disturbances.

Serum calcium levels may be reduced; in very rare cases tetany has been observed. Nephrolithiasis/ Nephrocalcinosis has been reported in premature infants.

Serum cholesterol (reduction of serum HDL-cholesterol, elevation of serum LDL-cholesterol) and triglyceride levels may rise during furosemide treatment. During long term therapy they will usually return to normal within six months.

As with other diuretics, treatment with Furosemide may lead to transitory increase in blood creatinine and urea levels. Serum levels of uric acid may increase and attacks of gout may occur.

The diuretic action of furosemide may lead to or contribute to hypovolaemia and dehydration, especially in elderly patients. Severe fluid depletion may lead to haemoconcentration with a tendency for thromboses to develop.

**General disorders and administration site conditions:**

Uncommon: Fatigue

Rare:
- severe anaphylactic or anaphylactoid reactions (e.g. with shock) occur rarely.
- fever
- malaise

**Gastrointestinal disorders:**

Uncommon: dry mouth, thirst, nausea, bowel motility disturbances, vomiting, diarrhoea, constipation.

Rare: Acute Pancreatitis

The gastro-intestinal disorders such as nausea or gastric upset (vomiting or diarrhoea) and constipation are not usually severe enough to necessitate withdrawal of treatment.

**Renal and urinary disorders:**
Uncommon:
- serum creatinine and urea levels can be temporarily elevated during treatment with furosemide.

Rare: interstitial nephritis, acute renal failure.

Increased urine production, urinary incontinence, can be caused or symptoms can be exacerbated in patients with urinary tract obstruction. Acute urine retention, possibly accompanied by complications, can occur for example in patients with bladder disorders, prostatic hyperplasia or narrowing of the urethra.

**Pregnancy, puerperium and perinatal conditions**
In premature infants with respiratory distress syndrome, administration of Furosemide Tablets in the initial weeks after birth entails an increased risk of a persistent patent ductus arteriosus.
In premature infants, furosemide can be precipitated as nephrocalcinosis/kidney stones.

Rare complications may include minor psychiatric disturbances.

**Reporting of suspected adverse reactions:**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

**4.9 Overdose**

Overdosage with furosemide results in dehydration, and electrolyte depletion due to excessive diuresis.

Symptoms include dehydration, volume depletion, electrolyte depletion and hypotension and cardiac toxicity due to excessive diuresis. In cirrhotic patients, overdosage may precipitate hepatic coma. The clinical picture in acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss, e.g. hypovolaemia, dehydration, haemoconcentration, cardiac arrhythmias due to excessive diuresis. Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion. High doses have the potential to cause transient deafness and may precipitate gout (disturbed uric acid secretion).

**Management**
The benefit of gastric decontamination is uncertain. Consider activated charcoal (50g for adults; 1g/kg for children) if an adult or child presents within 1 hour of ingesting a toxic dose. Treatment should be aimed at fluid replacement and correction of the electrolyte imbalance. The drug should be discontinued and electrolyte and water replacement instituted immediately; adjustment should be on the basis of careful monitoring.
• Observe for a minimum of 4 hours - monitor pulse and blood pressure.
• Treat hypotension and dehydration with appropriate IV fluids
• Monitor urinary output and serum electrolytes (including chloride and bicarbonate).

Correct electrolyte imbalances. Monitor 12 lead ECG in patients with significant electrolyte disturbances

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: High ceiling diuretics, sulphonamides, plain

ATC Code: CO3CA01

Furosemide is structurally related to thiazides, but its principal site of action is in the ascending limb of the loop of Henle. The loop diuretics like furosemide abolish the concentration gradient which is produced by thiazides acting in the cortex, when the fluid in the collecting tubules passes from the relatively hypotonic cortex, to the relatively hypertonic medulla and becomes concentrated. Furosemide probably also has effects along the entire nephron with the exception of the distal aldosterone-sensitive portion. It has a steep dose-response curve and progressive increase of dose causes progressive increase of urine production. Taken orally it acts within an hour and diuresis lasts about six hours. Enormous urine volumes, e.g. 10 litres in 24 hours can result and overdose can cause hypovolaemia and circulatory collapse. Given I.V., it acts within 30 minutes and can relieve acute pulmonary oedema, perhaps partially due to a vasodilator action which precedes the diuresis. An important feature of furosemide is its efficacy in the presence of glomerular filtration rates of 10ml/min or less as in severe heart failure and renal failure where the other diuretics fail.

5.2 Pharmacokinetic properties

Furosemide is completely, but fairly rapidly, absorbed from the gastro-intestinal tract. It has a biphasic half-life in the plasma, with a terminal elimination phase up to 1.5 hours, but this rises to over 10 hours in renal failure. It is up to 99 per cent bound to plasma proteins; and is mainly excreted in the urine, largely unchanged, but also in the form of the glucuronide and free amine metabolites. Variable amounts are excreted in the bile.

Furosemide crosses the placental barrier and is excreted in milk.
5.3 **Preclinical safety data**

There are no pre-clinical data of relevance to the prescriber that are additional to that already included in other sections of the SPC.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

- Lactose
- Pregelatinised maize starch
- Sodium starch glycollate
- Magnesium stearate
- Maize starch

6.2 **Incompatibilities**

None.

6.3 **Shelf life**

- 3 years for opaque plastic containers.
- 3 years for aluminium/opaque PVC blister packs.

6.4 **Special precautions for storage**

Store in the container provided. Do not store above 25°C.

Keep out of the reach and sight of children.

6.5 **Nature and contents of container**

Opaque plastic containers composed of polypropylene tubes and polyethylene tamper-evident closures in pack sizes of 28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1,000 tablets.
High density polypropylene or high density polyethylene containers with tamper-evident or child-resistant tamper-evident closures in pack sizes of 28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1,000 tablets.

PVC/Aluminium blister packs in pack sizes of 28, 30, 42, 56, 60, 84, 90 and 112 tablets.

6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER
Crescent Pharma Limited
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Polhampton Lane
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RG25 3ED
United Kingdom

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